

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF: Jotham Coe

APPLICATION NO.: 10/075,348

FILING DATE: February 14, 2002

TITLE: Aryl Fused Azapolycyclic Compounds

Examiner: Brenda Coleman

Group Art Unit: 1624

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Exhibit
Sir:

RULE 132 DECLARATION

I, Dane Liston, hereby, declare, state and say that:

- 1) I received a Ph.D. in Biochemical Pharmacology and Toxicology from the University of Utah in 1981.
- 2) I am currently employed by Pfizer, Inc. in Pfizer's Research and Development Division as a Associate Research Fellow in the Department of Neuroscience in Bldg 220 Rm 4362 and I have worked as a research scientist at Pfizer for 18 years.
- 3) I am familiar with the subject matter of the above identified application and the references cited therein. Particularly, I am familiar with claim 1, which recites the combination of a compound of formula I with either a muscarinic agonist or an amyloid aggregation inhibitor.
- 4) As one skilled in the art, I am very familiar with these aforementioned terms, and based on having read the application, I can readily identify specific members of any of the aforementioned narrow classes. For example, xanomeline, talsaclidine, YM796, AF102B are muscarinic agonists, and rifampicin and 4-iodo-4-deoxydoxorubicin are amyloid aggregation inhibitors. I could then readily formulate these with compounds of the instant formula I using the disclosure of the subject application and principles and procedures that are common knowledge in the art.

5) For more specific examples of the aforementioned classes, please see the following references, which were known in the art before the filing date of the application:

Muscarinic Agonists

1. Hollander E. Davidson M. Mohs RC. Horvath TB. Davis BM. Zemishlany Z. Davis KL. RS 86 in the treatment of Alzheimer's disease: cognitive and biological effects. *Biological Psychiatry*. 22(9):1067-78, 1987 Sep.
2. Fisher A. Heldman E. Gurwitz D. Haring R. Karton Y. Meshulam H. Pittel Z. Marciano D. Brandeis R. Sadot E. Barg Y. Pinkas-Kramarski R. Vogel Z. Ginzburg I. Treves TA. Verchovsky R. Klimowsky S. Korczyn AD. M1 agonists for the treatment of Alzheimer's disease. Novel properties and clinical update. *Annals of the New York Academy of Sciences*. 777:189-96, 1996 Jan 17.
3. Nakahara N. Iga Y. Saito Y. Mizobe F. Kawanishi G. Beneficial effects of FKS-508 (AF102B), a selective M1 agonist, on the impaired working memory in AF64A-treated rats. *Japanese Journal of Pharmacology*. 51(4):539-47, 1989 Dec.
4. Bromidge SM. Brown F. Cassidy F. Clark MS. Dabbs S. Hadley MS. Hawkins J. Loudon JM. Naylor CB. Orlek BS. Riley GJ. Design of [R-(Z)]-(+)-alpha-(methoxyimino)-1-azabicyclo[2.2.2]octane-3-acetonitrile (SB 202026), a functionally selective azabicyclic muscarinic M1 agonist incorporating the N-methoxy imidoyl nitrile group as a novel ester bioisostere. *Journal of Medicinal Chemistry*. 40(26):4265-80, 1997 Dec 19.
5. Bodick NC. Offen WW. Shannon HE. Satterwhite J. Lucas R. van Lier R. Paul SM. The selective muscarinic agonist xanomeline improves both the cognitive deficits and behavioral symptoms of Alzheimer disease. *Alzheimer Disease & Associated Disorders*. 11 Suppl 4:S16-22, 1997.
6. Plate R. Plaum MJ. de Boer T. Andrews JS. Rae DR. Gibson S. Synthesis and muscarinic activities of 3-(pyrazolyl)-1,2,5,6-tetrahydropyridine derivatives. *Bioorganic & Medicinal Chemistry*. 4(2):227-37, 1996 Feb.
7. Fisher A. Heldman E. Gurwitz D. Haring R. Karton Y. Meshulam H. Pittel Z. Marciano D. Brandeis R. Sadot E. Barg Y. Pinkas-Kramarski R. Vogel Z. Ginzburg I. Treves TA. Verchovsky R. Klimowsky S. Korczyn AD. M1 agonists for the treatment of Alzheimer's disease. Novel properties and clinical update. *Annals of the New York Academy of Sciences*. 777:189-96, 1996 Jan 17.

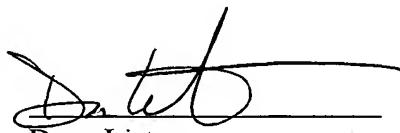
Amyloid Aggregation Inhibitors

1. Emmerling MR. Spiegel K. Watson MD. Inhibiting the formation of classical C3-convertase on the Alzheimer's beta-amyloid peptide. *Immunopharmacology*. 38(1-2):101-9, 1997 Dec.
2. Carr DB. Goate A. Phil D. Morris JC. Current concepts in the pathogenesis of Alzheimer's disease. *American Journal of Medicine*. 103(3A):3S-10S, 1997 Sep 22.
3. Parnetti L. Senin U. Mecocci P. Cognitive enhancement therapy for Alzheimer's disease. The way forward. *Drugs*. 53(5):752-68, 1997 May.
4. Merlini, G., Ascari, E., Amboldi, N., Bellotti, V., Arbustini, E., Perfetti, V., Ferrari, M., Zorzoli, I., Marinone, M. G., Garini, P. et al., Interaction of the anthracycline 4'-iodo-4'-deoxydoxorubicin with amyloid fibrils: inhibition of amyloidogenesis. *Proc Natl Acad Sci U S A*, 92(7): p. 2959-63. 1995.
5. Tomiyama, T., Asano, S., Suwa, Y., Morita, T., Kataoka, K., Mori, H., Endo, N. Rifampicin prevents the aggregation and neurotoxicity of amyloid beta protein in vitro. *Biochem Biophys Res Commun*, 204(1): p. 76-83, 1994.

6) Further declarant sayeth not.

I further declare that all statements made herein of my own knowledge are true and all statements made on information and belief to be true. All statements made herein are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under section 1001 of Title 18 of the United States Code, and that willful false statements may jeopardize the validity of the above application or any patent that may issue from it.

Date: 27 March, 2006



Dane Liston